



Source: Eikon Thomson Reuters

Market data

EPIC/TKR	AVCT
Price (p)	65.5
12m High (p)	98.0
12m Low (p)	60.0
Shares (m)	69.0
Mkt Cap (£m)	45.2
EV (£m)	32.0
Free Float*	59%
Market	AIM

*As defined by AIM Rule 26

Description

Avacta is a pre-clinical stage biotechnology company developing biotherapeutics based on its proprietary Affimer protein technology. It benefits from near-term revenues from research and diagnostic reagents.

Company information

CEO	Alastair Smith
CFO	Tony Gardiner
Chairman	Trevor Nicholls
	+44 1904 217 046
	www.avacta.com

Key shareholders

Directors	4.2%
IP Group	24.8%
Lombard Odier	11.5%
Aviva	9.8%
Baillie Gifford	6.6%
Ruffer LLP	7.1%

Diary

7 Feb	Capital Markets day
Apr-18	Interims
1H-18	Sloan Kettering feasibility

Analysts

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Avacta

Gene delivery collaboration

Avacta is the proprietary owner of Affimer technology for the development of biotherapeutics, diagnostic tests and research reagents. Affimers represent a radical alternative to antibody technology which dominates the drug industry. Avacta has made considerable progress towards its strategic goal to be ready to enter first-in-man Affimer trials by the end of 2019. It is also using external collaborations to expand the opportunities for Affimer technology. Avacta has now announced a tie-up with OncoSec Medical Inc to combine Affimers with the ImmunoPulse® electroporation technology to deliver Affimer therapies directly into tumours.

- **Strategy:** To commercialise its Affimer technology through a combination of bespoke research tools, collaborative deals and by identifying and developing its own proprietary therapeutic Affimer leads. Avacta has sufficient cash resources to identify an Affimer lead to be ready for first-in-man in 2019.
- **Electroporation:** A transfection technology in which a momentary electrical field is applied to cells in order to increase the permeability of the cell membrane by the creation of small pores, thereby allowing the delivery of genes that encode therapeutic proteins directly into the cell.
- **Collaboration:** Avacta has signed a collaboration agreement with OncoSec Medical to investigate the use of ImmunoPulse as a means of injecting Affimers directly into tumours. The tumour then produces clinically-relevant doses of the Affimer drug highly targeted in the tumour microenvironment.
- **Costs and outcomes:** Each party will bear its respective internal costs and will share all third-party costs associated with the partnership. Expectations are that the combined technologies can be used to create high-value immunotherapy combinations for clinical development and/or licensing deals.
- **Investment summary:** Avacta has made considerable progress towards its goal of having its own proprietary Affimer-based drugs and growing a profitable reagents business. By itself, AVCT has identified potential leads and completed both *in vitro* and *in vivo* pharmacokinetic pre-clinical tests, efficacy and immunogenicity tests. This collaboration has the potential to satisfy the need to get clinically-relevant doses of drug directly into tumours

Financial summary and valuation

Year-end July (£m)	2015	2016	2017	2018E	2019E	2020E
Sales	1.81	2.17	2.74	3.25	3.70	5.60
R&D spend	-0.03	-0.86	-1.95	-3.80	-4.30	-4.50
EBITDA	-2.28	-4.15	-6.01	-7.97	-8.42	-9.40
Underlying EBIT	-2.85	-4.75	-6.94	-8.91	-9.35	-10.33
Reported EBIT	-5.57	-5.66	-7.33	-10.13	-10.77	-11.84
Underlying PBT	-2.83	-4.65	-6.86	-8.86	-9.35	-10.38
Statutory PBT	-5.54	-5.57	-7.24	-10.09	-10.77	-11.89
Underlying EPS (p)	-4.38	-5.51	-7.79	-10.71	-11.09	-12.57
Statutory EPS (p)	-9.84	-6.86	-8.36	-12.50	-13.16	-14.78
Net (debt)/cash	7.33	19.52	13.17	4.05	-5.51	-15.96
Capital increase	0.02	21.05	0.01	0.00	0.00	0.00
EV/sales (x)	36.1	30.3	23.9	20.2	17.7	11.7

Source: Hardman & Co Life Sciences Research

Gene delivery collaboration

Avacta plc (AIM: AVCT) and OncoSec Medical Inc (NASDAQ: ONCS) have announced a research collaboration to investigate the use of OncoSec’s gene delivery technology, ImmunoPulse, as a method by which Avacta’s Affimers could be introduced directly into cells *in vivo*.

Avacta

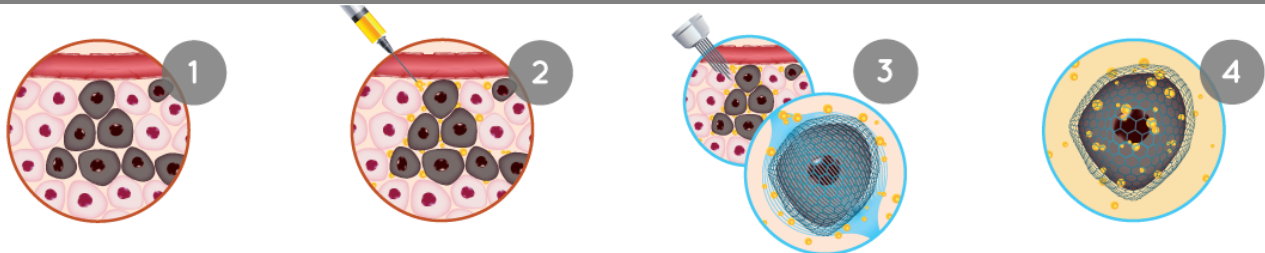
Over the last 18 months, Avacta has made considerable progress towards its goal of having its own proprietary Affimer-based drugs, which would represent a novel engineered alternative to antibodies. Avacta has identified immuno-oncology as a therapeutic area that would benefit from the numerous advantages of Affimers, with its lead product being AVA04, a PD-L1 inhibitor. The aim is to use ImmunoPulse to deliver such compounds directly into tumour cells in clinically meaningful doses.

OncoSec Medical

To date, OncoSec’s immunotherapy platform, ImmunoPulse, has been used in proof-of-concept studies to deliver, safely and efficiently, the gene for interleukin-12 (IL-12) a naturally-occurring protein with immune-stimulating characteristics, directly into patients’ tumours, as demonstrated in the graphic below.

The aim of this approach is to inject the DNA (or “gene”) that encodes a protein drug, which may be antibodies or Affimers, directly into cells in the patient’s body. These cells may be the tumour cells themselves to produce a localised dose of the drug or could be muscle cells which leads to a systemic dose throughout the body.

ImmunoPulse – OncoMed Medical electroporation technique

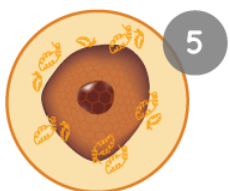


1 Cancer is identified in the body.

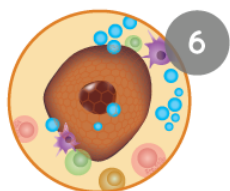
2 DNA-based interleukin-12 (IL-12), a naturally occurring protein, is injected directly into the tumor.

3 The applicator supplies a sequence of short-duration electrical pulses through a series of needles.

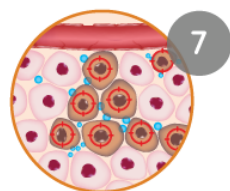
4 Electrical pulses result in increased permeability of the cell membrane, allowing DNA-based IL-12 to enter.



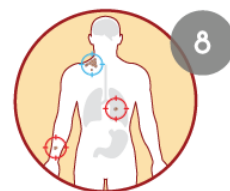
5 DNA-based IL-12 is expressed in the local tumor microenvironment.



6 IL-12 drives local inflammatory response in the tumor.



7 Immune cells are educated to recognize the patient's cancer.



8 Educated immune cells identify and attack tumors throughout the body.

Source: OncoSec Medical Inc

Electroporation (EP)

When high-amplitude, short-duration pulsed electric fields are applied to cells and tissues, the permeability of the cell membranes and tissue is increased. This increase in permeability has been explained by the temporary appearance of aqueous pores within the cell membrane, a phenomenon termed electroporation¹. The DNA or gene of a protein drug can be injected through these pores and once within the cell the DNA will be decoded and the cell will make the drug.

EP has been demonstrated to increase the cellular uptake of DNA plasmids by at least 1,000-fold compared to the delivery of 'naked DNA' alone, which means that much smaller doses of DNA are required to get good uptake and for a clinically relevant dose of drug to be made in the cells. The drug may then act within the cell or be ejected to have a wider effect in the local environment or across the whole body.

Advantages

- ▶ **Versatility:** Effective with nearly all cell and species types
- ▶ **Efficiency:** A high percentage (>80%) of cells are transfected with the target DNA/protein/gene without jeopardising viability of the cell
- ▶ **Small scale:** Uses much lower amounts of material

Disadvantages

- ▶ **Cell damage:** If electric pulses are wrong length or too intense, cell membrane pores may not close causing cell to rupture
- ▶ **Non-specific:** Any material can enter cell at the time of electro-permeability, making it non-specific, which could lead to improper cell function and cell death

Why Affimers for gene delivery?

The high degree of interest in the Affimer platform for gene delivery is because Affimers are easily expressed (made) by cells given that they have such a simple structure compared with antibodies and other alternatives, which means that a clinically-relevant dose is more easily achieved, and because of their small size. A large protein requires a large piece of nucleic acid (DNA or mRNA) to encode it and with some gene delivery approaches there is a limit to the size of nucleic acid that can be used, making it difficult or impossible to use large monoclonal antibodies. Affimers are ten times smaller than antibodies so it is possible to consider gene delivery of Affimers as monomers, dimers or higher order structures.

This partnership with OncoSec Medical is the third collaboration in the gene delivery area – the other two being with Moderna Therapeutics Inc (mRNA delivery of Affimers) and FIT Biotech (DNA delivery of Affimers). If these partnerships go well, then Avacta could establish the Affimer technology as the platform of choice for gene delivery.

Conclusion

Expectations from the two companies are that the results from this collaboration will demonstrate the potential of the combined technologies to create high-value immunotherapy combinations for clinical development and/or licensing.

Affimer® is a registered Trade Mark of Avacta plc
ImmunoPulse® is a registered Trade Mark of OncoSec Medical Inc.

¹ Yarmush et al 2014

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In particular, Article 12(3) of the Directive states: 'The following benefits shall qualify as acceptable minor non-monetary benefits only if they are' (b) 'written material from a third party that is commissioned and paid for by an[sic] corporate issuer or potential issuer to promote a new issuance by the company, or where the third party firm is contractually engaged and paid by the issuer to produce such material on an ongoing basis, provided that the relationship is clearly disclosed in the material and that the material is made available at the same time to any investment firms wishing to receive it or to the general public;'

The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: <http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf>

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